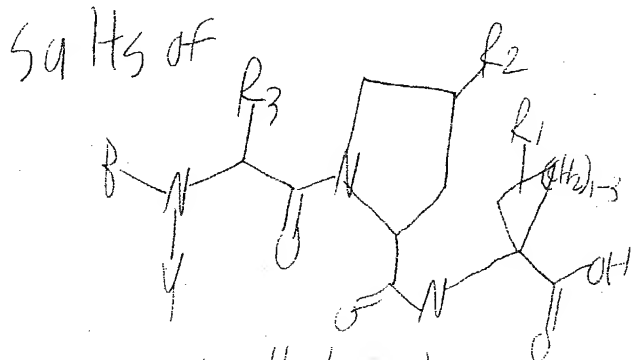


SEARCH REQUEST FORM

Requestor's Name: Edward Ward Serial Number: 10/620408
Date: Feb. 22, 2004 Phone: 571-272-0586 Art Unit: 1654
3D14 3D11

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).



R is H, alkyl, aryl
Hal, or alkyl-H, R₄C, R₄OC
R₄ is alkyl

as antiviral agents

R₃ is alkyl in a self-emulsifying formulation
R₂ is Quinolone Y is H, or alkyl
X is CH₂NH₂, O, or S
R₁ is H, or alkyl

STAFF USE ONLY

Date completed: 2/26/04
Searcher: Shapoval
Terminal time: _____
Elapsed time: _____
CPU time: _____
Total time: _____
Number of Searches: _____
Number of Databases: _____

Search Site
____ STIC
____ CM-1
____ Pre-S
Type of Search
____ N.A. Sequence
____ A.A. Sequence
____ Structure
____ Bibliographic

Vendors
____ IG
____ STN
____ Dialog
____ APS
____ Geninfo
____ SDC
____ DARC/Questel
____ Other



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 114860

TO: Edward Ward
Location: REM/3D14/3D11
Art Unit: 1654
February 25, 2004

Case Serial Number: 10/620408

From: P. Sheppard
Location: Remsen Building
Phone: (571) 272-2529

sheppard@uspto.gov

Search Notes

10/620,408

=> fil hcaplus
 FILE 'HCAPLUS' ENTERED AT 07:43:15 ON 26 FEB 2004
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 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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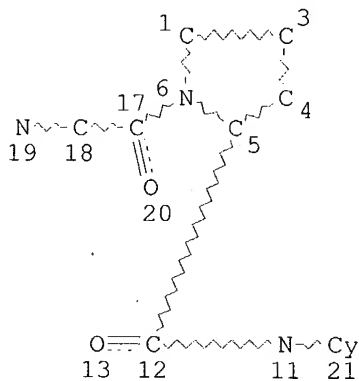
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FILE COVERS 1907 - 26 Feb 2004 VOL 140 ISS 9
 FILE LAST UPDATED: 25 Feb 2004 (20040225/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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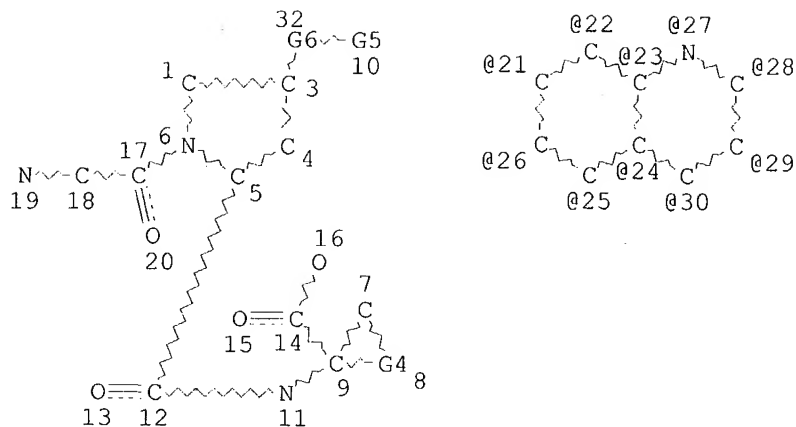
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 L11 STR



NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 13

STEREO ATTRIBUTES: NONE
 L13 2728 SEA FILE=REGISTRY SSS FUL L11
 L14 STR



REP G4=(1-3) C
 VAR G5=21/22/27/28/29/30/25/26/23/24
 REP G6=(0-1) A
 NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE

L15 341 SEA FILE=REGISTRY SUB=L13 SSS FUL L14
 L16 19 SEA FILE=HCAPLUS ABB=ON PLU=ON L15

=>

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=> d ibib abs hitrn l16 1-19

L16 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:960534 HCAPLUS

TITLE: NMR Structural Characterization of Peptide Inhibitors
 Bound to the Hepatitis C Virus NS3 Protease: Design of
 a New P2 Substituent

AUTHOR(S): Goudreau, Nathalie; Cameron, Dale R.; Bonneau, Pierre;
 Gorys, Vida; Plouffe, Celine; Poirier, Martin;
 Lamarre, Daniel; Llinas-Brunet, Montse

CORPORATE SOURCE: Departments of Chemistry and Biological Sciences,
 Research & Development, Boehringer Ingelheim (Canada)
 Ltd., Laval, QC, H7S 2G5, Can.

SOURCE: Journal of Medicinal Chemistry (2004), 47(1), 123-132
 CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A comparative NMR conformational anal. of three distinct tetrapeptide
 inhibitors of the Hepatitis C NS3 protease that differ at the
 4-aryloxy-substituted P2 proline position was undertaken. Specifically,
 transferred nuclear Overhauser effect expts. in combination with
 restrained systematic conformational searches were used to characterize
 the orientation of the P2 aryl substituents of these inhibitors when bound
 to the NS3 protease. Differences between free and bound conformations
 were also investigated. Anal. of the results allowed the design of a new

P2 arom. substituent, which significantly increased the potency of our inhibitors. The bound conformation of a specific competitive inhibitor having this novel P2 substituent is also described, along with a model of this inhibitor bound to the NS3 protease. This NS3 protease/inhibitor complex model also supports a hypothetical stabilization role for the P2 residue of the substrates and/or inhibitors and further elucidates the subtle details of the binding of the P2 residue of substrate-based inhibitors.

IT 357293-12-0P 652160-87-7P 652160-88-8P
652160-90-2P 652160-91-3P

RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design of improved P2 substituent in peptide inhibitor of Hepatitis C virus NS3 protease)

IT 357293-13-1

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(of tetrapeptide inhibitors of Hepatitis C NS3 protease)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:950866 HCAPLUS

DOCUMENT NUMBER: 140:16976

TITLE: Preparation of peptide heterocyclic sulfonamide
derivatives as hepatitis C virus inhibitors

INVENTOR(S): Campbell, Jeffrey Allen; Good, Andrew Charles

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 112 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

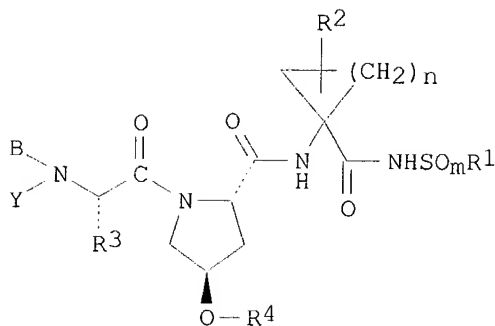
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2003099316 | A1 | 20031204 | WO 2003-US15786 | 20030520 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: US 2002-382104P P 20020520

OTHER SOURCE(S): MARPAT 140:16976

GI



I

AB The invention relates to tripeptide compds. I [R1 = (un)substituted heterocyclyl; m, n = 1 or 2; R2 = H, (halo)alk(en)yl, (halo)cycloalkyl, or together with the carbon atom to which it is attached forms a ring; R3 = (un)substituted alkyl or together with the carbon atom to which it is attached forms cycloalkyl optionally substituted by alkenyl; R4 = 7-methoxy-2-phenyl-4-quinolinyl; Y = H, (nitro)phenyl, (nitro)pyridyl, alkyl optionally substituted with cyano, OH, or cycloalkyl; B = H, alkyl, acyl, (thio)carbamoyl, sulfonyl, or sulfamoyl groups] or their pharmaceutically-acceptable salts for the treatment of hepatitis C virus (HCV) infection. Thus, I [R1 = 2-thienyl, m = 2, n = 1, R2 = vinyl, R3 = tert-Bu, B = H, Y = tert-butoxycarbonyl; stereochem. of 2-vinyl-substituted cyclopropane ring is (1R,2S)] was prepd. by a multistep procedure and assayed for inhibition of HCV NS3/4A protease (IC50 and EC50 < 0.1 .mu.M).

IT 259216-88-1P 445305-90-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of peptide heterocyclic sulfonamide derivs. as hepatitis C virus inhibitors)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:950834 HCAPLUS

DOCUMENT NUMBER: 140:16975

TITLE: Preparation of peptides as hepatitis C virus inhibitors

INVENTOR(S): Wang, Xiangdong Alan; Sun, Li-Quang; Sit, Sing-Yuen; Sin, Ny; Scola, Paul Michael; Hewawasam, Piyasena; Good, Andrew Charles; Chen, Yan; Campbell, Jeffrey Allen

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 675 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2003099274 | A1 | 20031204 | WO 2003-US15755 | 20030520 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,

TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,
MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-382055P P 20020520
OTHER SOURCE(S): MARPAT 140:16975
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Peptides I [R1 = alkyl, cycloalkyl, alkylcycloalkyl; m, n = 1 or 2; R2 = H, (halo)alk(en)yl, (halo)cycloalkyl; R3 = (un)substituted alkyl or together with the carbon atom to which it is attached forms cycloalkyl optionally substituted by alkenyl; R4 = (un)substituted (hetero)aryl; X = O, S, SO, SO₂, OCH₂, CH₂O, NH; Y = H, (nitro)pyridyl, (nitro)phenyl, alkyl optionally substituted with cyano, OH, or cycloalkyl; B = H, alkyl, acyl, (thio)carbamoyl, sulfonyl, or sulfamoyl groups (with provisos)] or their pharmaceutically-acceptable salts or prodrugs were prepd. for the treatment of hepatitis C virus (HCV) infection. Thus, compd. II (Boc = tert-butoxycarbonyl) was prepd. by a multistep procedure and assayed for inhibition of HCV NS3/4A protease (IC₅₀ and EC₅₀ < 0.1 .mu.M).

IT 259215-52-6P 259215-54-8P 259216-01-8P
630424-25-8P 630424-29-2P 630424-30-5P
630424-31-6P 630424-37-2P 630424-38-3P
630424-40-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of peptides as hepatitis C virus inhibitors)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:777398 HCAPLUS

DOCUMENT NUMBER: 139:246223

TITLE: Preparation of tripeptides having a hydroxyproline ether of a substituted quinoline for the inhibition of hepatitis C virus (HCV) NS3 protease

INVENTOR(S): Llinas-Brunet, Montse; Gorys, Vida J.

PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany

SOURCE: U.S. Pat. Appl. Publ., 31 pp., Cont.-in-part of U.S. Ser. No. 321,218, abandoned.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

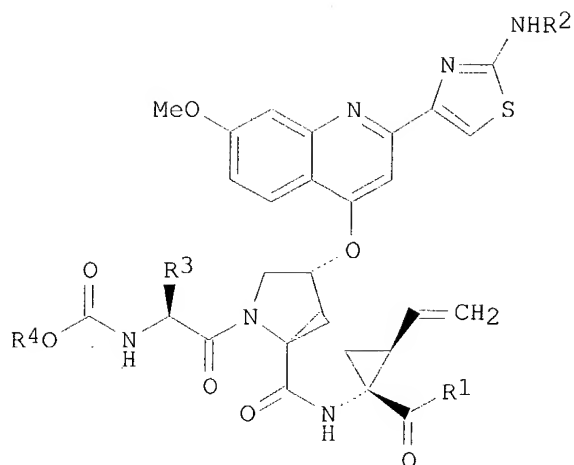
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2003187018 | A1 | 20031002 | US 2003-353589 | 20030129 |
| US 6642204 | B2 | 20031104 | | |

PRIORITY APPLN. INFO.: CA 2002-2370396 A 20020201
US 2002-321218 B2 20021217

OTHER SOURCE(S): MARPAT 139:246223
GI



I

AB Tripeptides I [R1 is OH or NHSO₂R_{1A}, where R_{1A} is (cyclo)alkyl, alkylcycloalkyl, or aryl which are optionally substituted from 1 to 3 times with halo, cyano, nitro, alkoxy, amido, etc.; R₂, R₄ are cycloalkyl; R₃ is t-Bu or cycloalkyl] or their pharmaceutically-acceptable salts were prep'd. as inhibitors of HCV NS3 protease. Thus, I (R₁ = OH, R₂, R₄ = cyclopentyl, R₃ = t-Bu) was prep'd. and shown to have IC₅₀ < 0.1 .mu.M in the NS3-NS4A protease assay and EC₅₀ < 0.5 .mu.M in the cell-based HCV RNA replication assay.

IT 572924-90-4P 572925-03-2P 572925-04-3P
572925-05-4P 572925-06-5P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of tripeptides having hydroxyproline ether of substituted quinoline for inhibition of HCV NS3 protease)

IT 572924-91-5P 572924-92-6P 572924-93-7P
572924-94-8P 572924-95-9P 572924-97-1P
572924-98-2P 572924-99-3P 572925-00-9P
572925-01-0P 572925-02-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of tripeptides having hydroxyproline ether of substituted quinoline for inhibition of HCV NS3 protease)

IT 572924-78-8P 572924-79-9P 572924-80-2P
572924-81-3P 572924-82-4P 572924-84-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of tripeptides having hydroxyproline ether of substituted quinoline for inhibition of HCV NS3 protease)

L16 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:777373 HCAPLUS

DOCUMENT NUMBER: 139:246222

TITLE: Preparation of heterocyclic tripeptides as hepatitis C inhibitors

INVENTOR(S): Llinas-Brunet, Montse; Bailey, Murray D.; Ghiro, Elise

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany

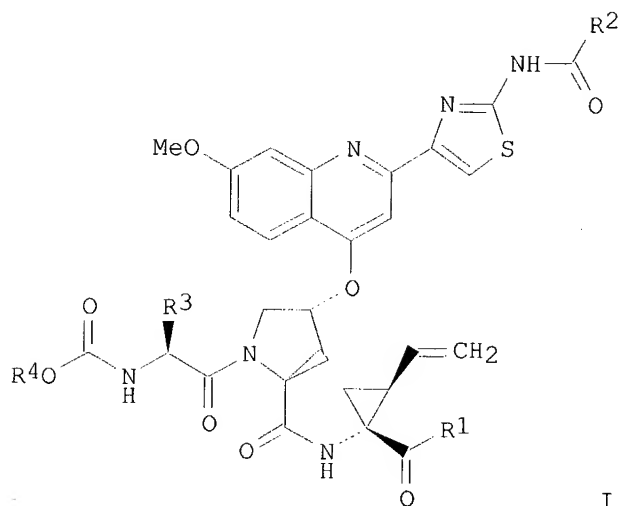
SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U.S. Ser. No. 320,979.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|-------------------|-----------------|-------------|
| US 2003186895 | A1 | 20031002 | US 2003-353563 | 20030129 |
| US 2003191067 | A1 | 20031009 | US 2002-320979 | 20021217 |
| PRIORITY APPLN. INFO.: | | | CA 2002-2369970 | A 20020201 |
| | | | US 2002-320979 | A2 20021217 |
| OTHER SOURCE(S): | | MARPAT 139:246222 | | |
| GI | | | | |



AB Tripeptides I [R1 is OH or NHSO₂R_{1A}, where R_{1A} is (cyclo)alkyl, alkylcycloalkyl, or aryl which are optionally substituted from 1 to 3 times with halo, cyano, nitro, alkoxy, amido, etc.; R₂ is t-Bu, t-BuCH₂, or cyclopentylmethyl; R₃ is t-Bu or cyclohexyl; R₄ is cyclobutyl, cyclopentyl, or cyclohexyl] or their pharmaceutically-acceptable salts were prepd. as inhibitors of the hepatitis C virus NS3 protease. Thus, I (R₁ = OH, R₂ = t-BuCH₂, R₃ = t-Bu, R₄ = cyclopentyl) was prepd. and shown to have IC₅₀ < 0.1 .mu.M in the NS3-NS4A protease assay and EC₅₀ < 0.5 .mu.M in the cell-based HCV RNA replication assay.

IT **572924-07-3P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (prepn. of heterocyclic tripeptides as hepatitis C inhibitors)

IT **572924-08-4P 572924-12-0P 572924-14-2P**

572924-16-4P 572924-18-6P 572924-21-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of heterocyclic tripeptides as hepatitis C inhibitors)

IT **572924-09-5**

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of heterocyclic tripeptides as hepatitis C inhibitors)

IT **572924-06-2P 572924-10-8P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of heterocyclic tripeptides as hepatitis C inhibitors)

L16 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:648255 HCAPLUS

DOCUMENT NUMBER: 139:197768

TITLE: Preparation of macrocyclic peptides active against the hepatitis C virus

INVENTOR(S): Tsantrizos, Youla S.; Cameron, Dale R.; Faucher, Anne-Marie; Ghiro, Elise; Goudreau, Nathalie; Halmos, Teddy; Llinas-Brunet, Montse

PATENT ASSIGNEE(S): Boehringer Ingelheim (Canada) Ltd., Can.

SOURCE: U.S., 90 pp., Cont.-in-part of U.S. Ser. No. 542,675, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

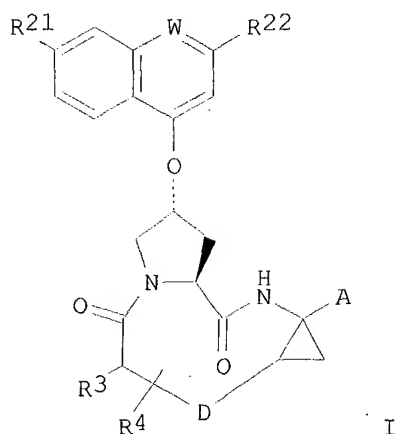
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 6608027 | B1 | 20030819 | US 2001-760946 | 20010116 |
| US 2004002448 | A1 | 20040101 | US 2003-358726 | 20030205 |
| PRIORITY APPLN. INFO.: | | | US 1999-128011P | P 19990406 |
| | | | US 2000-542675 | B2 20000403 |
| | | | US 2001-760946 | A1 20010116 |

OTHER SOURCE(S): MARPAT 139:197768

GI



AB Macrocyclic peptides I [W = CH or N; R21 = H, halo, alkyl, cycloalkyl, haloalkyl, alkoxy, cycloalkoxy, hydroxy, or an amino group; R22 = H, halo, alkyl, cycloalkyl, haloalkyl, thioalkyl, alkoxy, cycloalkoxy, alkoxyalkyl, cycloalkyl, aryl or heteroaryl; R3 = hydroxy, NH2, aryl- or heteroarylamino, NHCOR32, CONHR32, CO2R32, where R32 is alkyl or cycloalkyl; D is a 5 to 10-atom satd. or unsatd. alkylene chain optionally contg. one to three heteroatoms independently selected from: O, S, or NH or substituted imino; R4 = H or from one to three substituents at any carbon atom of chain D; A is an amide or carboxylic acid group or a pharmaceutically acceptable salt or ester; two diastereomers may exist at the cyclopropane moiety] were prepd. which are active in-vitro and in cellular assays against the NS3 protease of the hepatitis C virus. Thus, macrocyclic peptide I [W = N; R21, R22, R4 = H; A = CO2H; R3CH-D = (S)-(Me3CO2CNH)CH(CH2)3CH:CH(CH2)2-E (syn to acid)] was prepd. and showed

IC50 > 0.1 .mu.M in the full-length NS3-NS4A heterodimer protein
fluorogenic assay.

IT 300831-47-4 300831-62-3 300831-65-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of macrocyclic peptides active against the hepatitis C virus)

IT 300831-44-1P 300831-51-0P 300831-52-1P

300831-53-2P 300831-59-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(prepn. of macrocyclic peptides active against the hepatitis C virus)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:610479 HCAPLUS

DOCUMENT NUMBER: 139:164980

TITLE: Preparation of tripeptides having a hydroxyproline
ether of a substituted quinoline for the inhibition of
NS3 (hepatitis C)

INVENTOR(S): Llinas-Brunet, Montse; Gorys, Vida J.

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany

SOURCE: PCT Int. Appl., 56 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

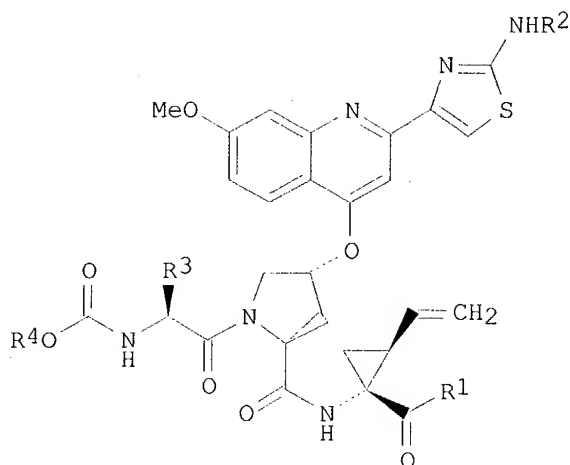
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2003064456 | A1 | 20030807 | WO 2003-CA90 | 20030124 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CQ, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: CA 2002-2370396 A 20020201

OTHER SOURCE(S): MARPAT 139:164980

GI



I

AB Tripeptides I [R1 is OH or NHSO2R1A, where R1A is (cyclo)alkyl, alkylcycloalkyl, or aryl which are optionally substituted from 1 to 3 times with halo, cyano, nitro, alkoxy, amido, etc.; R2, R4 are cycloalkyl; R3 is t-Bu or cycloalkyl] or their pharmaceutically-acceptable salts were prepd. as inhibitors of HCV NS3 protease for the treatment of hepatitis C. Thus, I (R1 = OH, R2, R4 = cyclopentyl, R3 = t-Bu) was prepd. and shown to have IC50 < 0.1 .mu.M in the NS3-NS4A protease assay and EC50 < 0.5 .mu.M in the cell-based HCV RNA replication assay.

IT 572924-90-4P 572925-03-2P 572925-04-3P
572925-05-4P 572925-06-5P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of tripeptides having a hydroxyproline ether of a substituted quinoline for the inhibition of NS3 (hepatitis C))

IT 572924-91-5P 572924-92-6P 572924-93-7P
572924-94-8P 572924-95-9P 572924-97-1P
572924-98-2P 572924-99-3P 572925-00-9P
572925-01-0P 572925-02-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of tripeptides having a hydroxyproline ether of a substituted quinoline for the inhibition of NS3 (hepatitis C))

IT 572924-78-8P 572924-79-9P 572924-80-2P
572924-81-3P 572924-82-4P 572924-84-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of tripeptides having a hydroxyproline ether of a substituted quinoline for the inhibition of NS3 (hepatitis C))

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:610444 HCAPLUS

DOCUMENT NUMBER: 139:164978

TITLE: Preparation of heterocyclic tripeptides as hepatitis C inhibitors

INVENTOR(S): Llinas-Brunet, Montse; Bailey, Murray D.; Ghio, Elise

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany

SOURCE: PCT Int. Appl., 42 pp.

CODEN: PIXXD2

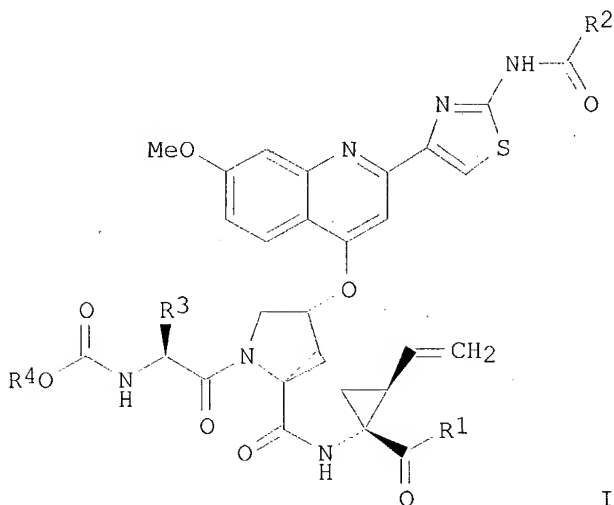
DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2003064416 | A1 | 20030807 | WO 2003-CA91 | 20030124 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: CA 2002-2369970 A 20020201

OTHER SOURCE(S): MARPAT 139:164978

GI



AB Tripeptides I [R1 is OH or NHSO2R1A, where R1A is (cyclo)alkyl, alkylcycloalkyl, or aryl which are optionally substituted from 1 to 3 times with halo, cyano, nitro, alkoxy, amido, etc.; R2 is t-Bu, t-BuCH2, or cyclopentylmethyl; R3 is t-Bu or cyclohexyl; R4 is cyclobutyl, cyclopentyl, or cyclohexyl] or their pharmaceutically-acceptable salts were prepd. as inhibitors of the hepatitis C virus NS3 protease. Thus, I (R1 = OH, R2 = t-BuCH2, R3 = t-Bu, R4 = cyclopentyl) was prepd. and shown to have IC50 < 0.1 .mu.M in the NS3-NS4A protease assay and EC50 < 0.5 .mu.M in the cell-based HCV RNA replication assay.

IT 572924-07-3P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (prepn. of heterocyclic tripeptides as hepatitis C inhibitors)

IT 572924-08-4P 572924-12-0P 572924-14-2P
 572924-16-4P 572924-18-6P 572924-21-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of heterocyclic tripeptides as hepatitis C inhibitors)

IT 572924-09-5

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of heterocyclic tripeptides as hepatitis C inhibitors)

IT 572924-06-2P 572924-10-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of heterocyclic tripeptides as hepatitis C inhibitors)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:535070 HCAPLUS

DOCUMENT NUMBER: 139:292471

TITLE: Novel, potent phenethylamide inhibitors of the hepatitis C virus (HCV) NS3 protease: probing the role of P2' aryloxyprolines with hybrid structures

AUTHOR(S): Orvieto, Federica; Koch, Uwe; Matassa, Victor G.; Muraglia, Ester

CORPORATE SOURCE: Medicinal Chemistry Department, IRBM-MRL Rome, Rome, 00040, Italy

SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(16), 2745-2748

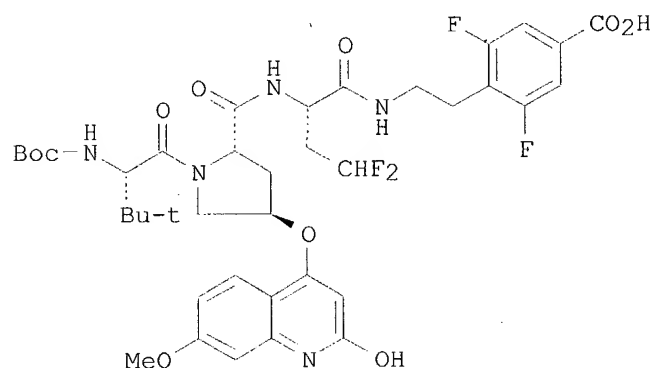
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB Synthesis of hybrid HCV NS3 protease/NS4A inhibitors having the 4,4-difluoroaminobutyric acid (difluoroAbu) phenethylamides as P1-P1' and quinolyloxyprolines as P2 fragments led to I (Boc = tert-butoxycarbonyl) (IC50 54 nM). Mol. modeling suggests that this potent tripeptide inhibitor utilizes interactions in the S1', S1, S2, S3 and S4 sites of the protease.

IT 259215-38-8 607403-39-4

RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)

(prepn. and structure-protease-inhibiting activity relationship of phenethylamide peptidomimetics)

IT 259216-88-1P

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. and structure-protease-inhibiting activity relationship of
phenethylamide peptidomimetics)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:511084 HCAPLUS
DOCUMENT NUMBER: 139:69527
TITLE: Preparation of macrocyclic compounds as inhibitors of
hepatitis C virus
INVENTOR(S): Campbell, Jeffrey Allen; Good, Andrew Charles
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 225 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2003053349 | A2 | 20030703 | WO 2002-US39926 | 20021213 |
| WO 2003053349 | A3 | 20040115 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-344080P P 20011220
US 2002-382103P P 20020520

OTHER SOURCE(S): MARPAT 139:69527
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to macrocyclic compds. I [R1 = (cyclo)alkyl; R2 = H, halo, alkyl, alkoxy, cycloalkoxy, (un)substituted aryl or heterocyclyl; R3 = H, halo, CF3, alkoxy, cycloalkoxy; R4 = NH2 or NHR6, where R6 is alkanoyl, alkylaminocarbonyl, or carbalkoxy; Q is a 3-9 atom (un)satd. alkylene chain optionally contg. 1-3 heteroatoms O, S, SO, or SO2], including methods for their synthesis and use in pharmaceutical compns. for therapeutic or prophylactic prevention or treatment of hepatitis C virus (HCV) infection. Thus, 3,13-diazatricyclo[11.3.0.04,6]hexadec-7-ene deriv. II was prepd. by a multistep procedure and assayed for inhibition of HCV NS3/4A protease (IC50 < 5 .mu.M).

IT 300831-62-3P 552335-25-8P 552335-28-1P
552335-31-6P

RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of macrocyclic compds. as inhibitors of hepatitis C virus)

IT 552335-48-5P 552335-52-1P 552335-56-5P
552335-61-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(prepn. of macrocyclic compds. as inhibitors of hepatitis C virus)

L16 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:403023 HCAPLUS

DOCUMENT NUMBER: 139:173244

TITLE: An NS3 Serine Protease Inhibitor Abrogates Replication of Subgenomic Hepatitis C Virus RNA

AUTHOR(S): Pause, Arnim; Kukolj, George; Bailey, Murray; Brault, Martine; Do, Florence; Halmos, Ted; Lagace, Lisette; Maurice, Roger; Marquis, Martin; McKercher, Ginette; Pellerin, Charles; Pilote, Louise; Thibeault, Diane; Lamarre, Daniel

CORPORATE SOURCE: Department of Biological Sciences, Boehringer Ingelheim (Canada) Ltd., Research and Development, Laval, QC, H7S 2G5, Can.

SOURCE: Journal of Biological Chemistry (2003), 278(22), 20374-20380

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The hepatitis C virus (HCV) NS3 protease is essential for polyprotein maturation and viral propagation, and it has been proposed as a suitable target for antiviral drug discovery. An N-terminal hexapeptide cleavage product of a dodecapeptide substrate identified as a weak competitive inhibitor of the NS3 protease activity was optimized to a potent and highly specific inhibitor of the enzyme. The effect of this potent NS3 protease inhibitor was evaluated on replication of subgenomic HCV RNA and compared with interferon- α . (IFN- α), which is currently used in the treatment of HCV-infected patients. Treatment of replicon-contg. cells with the NS3 protease inhibitor or IFN- α showed a dose-dependent decrease in subgenomic HCV RNA that reached undetectable levels following a 14-day treatment. Kinetic studies in the presence of either NS3 protease inhibitor or IFN- α also revealed similar profiles in HCV RNA decay with half-lives of 11 and 14 h, resp. The finding that an antiviral specifically targeting the NS3 protease activity inhibits HCV RNA replication further validates the NS3 enzyme as a prime target for drug discovery and supports the development of NS3 protease inhibitors as a novel therapeutic approach for HCV infection.

IT 579472-70-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(NS3 serine protease inhibitor abrogates replication of subgenomic hepatitis C virus RNA)

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:338309 HCAPLUS

DOCUMENT NUMBER: 139:143358

TITLE: Macrocyclic inhibitors of the NS3 protease as potential therapeutic agents of hepatitis C virus infection

AUTHOR(S): Tsantrizos, Youla S.; Bolger, Gordon; Bonneau, Pierre; Cameron, Dale R.; Goudreau, Nathalie; Kukolj, George; LaPlante, Steven R.; Llinas-Brunet, Montse; Nar, Herbert; Lamarre, Daniel

CORPORATE SOURCE: Departments of Chemistry and Biological Sciences Research and Development, Boehringer Ingelheim (Canada) Ltd., Laval, QC, H7S 2G5, Can.

SOURCE: Angewandte Chemie, International Edition (2003),

42(12), 1356-1360

CODEN: ACIEF5; ISSN: 1433-7851

PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A novel class of selective inhibitors of the hepatitis C virus NS3 protease, an enzyme which is essential for viral replication in vivo, was developed. The inhibitors are based on the structure-activity relationship between a substrate-based peptidomimetic ligand and the HCV NS3 serine protease. The designed HCV inhibitor and its satd. analogs are the first inhibitors of the NS3 protease which inhibit HCV RNA replication in the cell-based replicon assay. In addn., they are orally absorbed and stable to metabolic breakdown. Thus, these compds. show many of the desirable properties of a druglike archetype and could lead t a clin. useful antiviral agent for the treatment of hepatitis C viral infections in humans.

IT 357293-16-4P 572918-58-2P 572918-60-6P

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(macrocyclic inhibitors of the NS3 protease as potential therapeutic agents of hepatitis C virus infection)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:199010 HCAPLUS

DOCUMENT NUMBER: 139:223763

TITLE: In vitro selection and characterization of hepatitis C virus serine protease variants resistant to an active-site peptide inhibitor

AUTHOR(S): Trozzi, Caterina; Bartholomew, Linda; Ceccacci, Alessandra; Biasiol, Gabriella; Pacini, Laura; Altamura, Sergio; Narjes, Frank; Muraglia, Ester; Paonessa, Giacomo; Koch, Uwe; De Francesco, Raffaele; Steinkuhler, Christian; Migliaccio, Giovanni

CORPORATE SOURCE: IRBM "P. Angeletti", Rome, 00040, Italy

SOURCE: Journal of Virology (2003), 77(6), 3669-3679

CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The hepatitis C virus (HCV) serine protease is necessary for viral replication and represents a valid target for developing new therapies for HCV infection. Potent and selective inhibitors of this enzyme have been identified and shown to inhibit HCV replication in tissue culture. The optimization of these inhibitors for clin. development would greatly benefit from in vitro systems for the identification and the study of resistant variants. We report the use HCV subgenomic replicons to isolate and characterize mutants resistant to a protease inhibitor. Taking advantage of the replicons' ability to transduce resistance to neomycin, we selected replicons with decreased sensitivity to the inhibitor by culturing the host cells in the presence of the inhibitor and neomycin. The selected replicons replicated to the same extent as those in parental cells. Sequence anal. followed by transfection of replicons contg. isolated mutations revealed that resistance was mediated by amino acid substitutions in the protease. These results were confirmed by in vitro expts. with mutant enzymes and by modeling the inhibitor in the three-dimensional structure of the protease.

IT 259215-49-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(in vitro selection and characterization of hepatitis C virus serine

protease variants resistant to an active-site peptide inhibitor using
HCV subgenomic replicons)

IT 259215-49-1D, complex with NS3-4A active site

RL: PRP (Properties)

(model of tripeptide inhibitor in NS3-4A protease active site; in vitro
selection and characterization of hepatitis C virus serine protease
variants resistant to an active-site peptide inhibitor using HCV
subgenomic replicons)

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:594872 HCAPLUS

DOCUMENT NUMBER: 137:155180

TITLE: Preparation of tripeptides as hepatitis C inhibitors

INVENTOR(S): Campbell, Jeffrey Allen; Good, Andrew

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 240 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

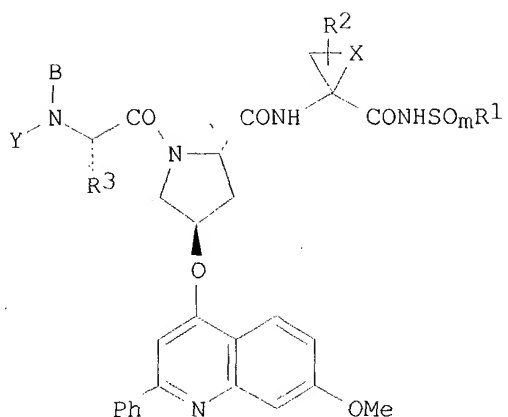
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2002060926 | A2 | 20020808 | WO 2001-US45145 | 20011120 |
| WO 2002060926 | A3 | 20030313 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| US 2002111313 | A1 | 20020815 | US 2001-1850 | 20011120 |
| EP 1337550 | A2 | 20030827 | EP 2001-997024 | 20011120 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |

PRIORITY APPLN. INFO.: US 2000-249968P P 20001120
WO 2001-US45145 W 20011120

OTHER SOURCE(S): MARPAT 137:155180

GI



I

AB Tripeptides I [R1 = (un)substituted alkyl, cycloalkyl, alkylcycloalkyl, or aryl; m = 1 or 2; X = CH₂ or CH₂CH₂; R2 = H or (un)substituted alkyl, alkenyl, or cycloalkyl; R3 = alkyl, phenylalkyl, alkenyl, (un)substituted cycloalkyl or alkylcycloalkyl CR3 is a cycloalkyl group optionally substituted by alkenyl; Y = H, nitrophenyl, nitropyridyl, or alkyl optionally substituted by cyano, hydroxyl, or cycloalkyl; B = H, alkyl, acyl, carbamoyl, thiocarbamoyl, or a sulfonyl group] were prepd. for the treatment of hepatitis C virus (HCV) infection. Synthetic procedures and biol. test data are given for 141 tripeptides I. Compd. I (R1 = p-AcNHC6H₄, m = 2, X = CH₂, R2 = vinyl, R3 = tert-Bu, B = H, Y = tert-butoxycarbonyl) showed IC₅₀ < 0.05 .mu.M for inhibition of HCV NS3/4A protease (BMS strain) and EC₅₀ < 0.5 .mu.M in the HCV replicon cell-based assay.

IT 445305-97-5

RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of tripeptides as hepatitis C inhibitors)

IT 259214-72-7P 259215-34-4P 259216-15-4P
259216-79-0P 259216-88-1P 445305-80-6P
445305-81-7P 445305-90-8P 445305-94-2P
445305-95-3P 445305-96-4P 445305-99-7P
445306-03-6P 445306-06-9P 445306-42-3P
445306-43-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. of tripeptides as hepatitis C inhibitors)

L16 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:435622 HCAPLUS

DOCUMENT NUMBER: 135:195782

TITLE: Solid-Phase Synthesis of Peptidomimetic Inhibitors for the Hepatitis C Virus NS3 Protease

AUTHOR(S): Poupard, Marc-Andre; Cameron, Dale R.; Chabot, Catherine; Ghiro, Elise; Goudreau, Nathalie; Goulet, Sylvie; Poirier, Martin; Tsantrizos, Youla S.

CORPORATE SOURCE: Department of Chemistry, Boehringer Ingelheim (Canada) Ltd., QC, H7S 2G5, Can.

SOURCE: Journal of Organic Chemistry (2001), 66(14), 4743-4751
CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:195782

AB The NS3 serine protease enzyme of the hepatitis C virus (HCV) is essential for viral replication. Short peptides mimicking the N-terminal substrate

cleavage products of the NS3 protease are known to act as weak inhibitors of the enzyme and have been used as templates for the design of peptidomimetic inhibitors. Automated solid-phase synthesis of a small library of compds. based on such a peptidomimetic scaffold has led to the identification of potent and highly selective inhibitors of the NS3 protease enzyme.

IT 357293-16-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(solid-phase synthesis of peptidomimetic inhibitors for the hepatitis C virus NS3 protease)

IT 357293-08-4P 357293-09-5P 357293-12-0P
357293-13-1P 357293-14-2P 357293-15-3P
357293-17-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(solid-phase synthesis of peptidomimetic inhibitors for the hepatitis C virus NS3 protease)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:725652 HCAPLUS

DOCUMENT NUMBER: 133:296659

TITLE: Preparation of macrocyclic peptides active against the hepatitis C virus

INVENTOR(S): Tsantrizos, Youla S.; Cameron, Dale R.; Faucher, Anne-marie; Ghire, Elise; Goudreau, Nathalie; Halmos, Teddy; Llinas-brunet, Montse

PATENT ASSIGNEE(S): Boehringer Ingelheim (Canada) Ltd., Can.

SOURCE: PCT Int. Appl., 154 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

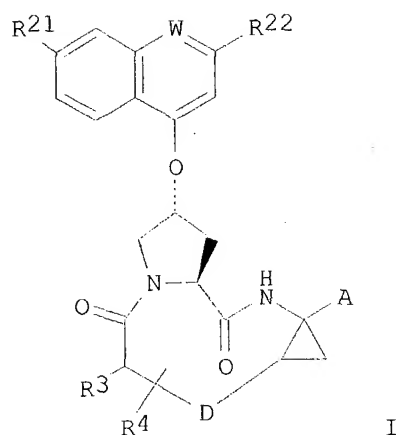
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2000059929 | A1 | 20001012 | WO 2000-CA353 | 20000403 |
| W: | | | | |
| AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: | | | | |
| GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1169339 | A1 | 20020109 | EP 2000-913999 | 20000403 |
| R: | | | | |
| AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| BR 2000009599 | A | 20020115 | BR 2000-9599 | 20000403 |
| EE 200100516 | A | 20021216 | EE 2001-516 | 20000403 |
| BG 105970 | A | 20020531 | BG 2001-105970 | 20011002 |
| HR 2001000720 | A1 | 20021231 | HR 2001-720 | 20011004 |
| NO 2001004857 | A | 20011031 | NO 2001-4857 | 20011005 |

PRIORITY APPLN. INFO.: US 1999-128011P P 19990406
WO 2000-CA353 W 20000403

OTHER SOURCE(S): MARPAT 133:296659

GI



AB Macrocylic peptides I [W = CH or N; R21 = H, halo, alkyl, cycloalkyl, haloalkyl, alkoxy, cycloalkoxy, hydroxy, or an amino group; R22 = H, halo, alkyl, cycloalkyl, haloalkyl, thioalkyl, alkoxy, cycloalkoxy, alkoxyalkyl, cycloalkyl, aryl or heteroaryl; R3 = hydroxy, NH₂, aryl- or heteroarylamino, NHCOR32, CONHR32, CO₂R32, where R32 is alkyl or cycloalkyl; D is a 5 to 10-atom satd. or unsatd. alkylene chain optionally contg. one to three heteroatoms independently selected from: O, S, or NH or substituted imino; R4 = H or from one to three substituents at any carbon atom of chain D; A is an amide or carboxylic acid group or a pharmaceutically acceptable salt or ester; two diastereomers may exist at the cyclopropane moiety] were prepd. which are active in-vitro and in cellular assays against the NS3 protease of the hepatitis C virus. Thus, macrocylic peptide I [W = N; R21, R22, R4 = H; A = CO₂H; R3CH-D = (S)-(Me₃CO₂CNH)CH(CH₂)₃CH:CH(CH₂)₂-E (syn to acid)] was prepd. and showed IC₅₀ > 0.1 .mu.M in the full-length NS3-NS4A heterodimer protein fluorogenic assay.

IT 300831-47-4 300831-62-3 300831-65-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of macrocylic peptides active against the hepatitis C virus)

IT 300831-44-1P 300831-51-0P 300831-52-1P

300831-53-2P 300831-59-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of macrocylic peptides active against the hepatitis C virus)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:133728 HCAPLUS

DOCUMENT NUMBER: 132:175808

TITLE: Hepatitis C inhibitor peptides

INVENTOR(S): Llinas-Brunet, Montse; Bailey, Murray D.; Cameron, Dale; Ghio, Elise; Goudreau, Nathalie; Poupart, Marc-Andre; Rancourt, Jean; Tsantrizos, Youla S.

PATENT ASSIGNEE(S): Boehringer Ingelheim (Canada) Ltd., Can.

SOURCE: PCT Int. Appl., 113 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

259221-54-0P 259221-55-1P 259221-56-2P
 259221-57-3P 259221-58-4P 259221-59-5P
 259221-60-8P 259221-61-9P 259221-62-0P
 259221-63-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (hepatitis C inhibitor peptides and prepn. thereof)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:133714 HCAPLUS

DOCUMENT NUMBER: 132:180871

TITLE: Preparation of hepatitis C inhibitory tripeptides

INVENTOR(S): Llinas-Brunet, Montse; Bailey, Murray D.; Cameron, Dale; Faucher, Anne-Marie; Ghio, Elise; Goudreau, Nathalie; Halmos, Teddy; Poupart, Marc-Andre; Rancourt, Jean; Tsantrizos, Youla S.; Wernic, Dominik M.; Simoneau, Bruno

PATENT ASSIGNEE(S): Boehringer Ingelheim (Canada) Ltd., Can.

SOURCE: PCT Int. Appl., 168 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-------------------|----------|
| WO 2000009543 | A2 | 20000224 | WO 1999-CA736 | 19990809 |
| WO 2000009543 | A3 | 20000525 | | |
| W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| US 6323180 | B1 | 20011127 | US 1999-368866 | 19990805 |
| CA 2338946 | AA | 20000224 | CA 1999-2338946 | 19990809 |
| AU 9952731 | A1 | 20000306 | AU 1999-52731 | 19990809 |
| BR 9913646 | A | 20010605 | BR 1999-13646 | 19990809 |
| EP 1105413 | A2 | 20010613 | EP 1999-938084 | 19990809 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | |
| JP 2002522554 | T2 | 20020723 | JP 2000-564993 | 19990809 |
| EE 200100081 | A | 20020815 | EE 2001-81 | 19990809 |
| US 6268207 | B1 | 20010731 | US 2000-660030 | 20000912 |
| US 6329379 | B1 | 20011211 | US 2000-675398 | 20000929 |
| US 6329417 | B1 | 20011211 | US 2000-703751 | 20001101 |
| BG 105232 | A | 20011130 | BG 2001-105232 | 20010208 |
| HR 2001000102 | A1 | 20020228 | HR 2001-102 | 20010208 |
| NO 2001000683 | A | 20010402 | NO 2001-683 | 20010209 |
| US 2002016442 | A1 | 20020207 | US 2001-827976 | 20010406 |
| US 6420380 | B2 | 20020716 | | |
| US 2002037998 | A1 | 20020328 | US 2001-849057 | 20010504 |
| US 6410531 | B2 | 20020625 | | |
| US 6534523 | B1 | 20030318 | US 2002-91293 | 20020305 |
| PRIORITY APPLN. INFO.: | | | US 1998-95931P P | 19980810 |
| | | | US 1999-132386P P | 19990504 |

US 1999-368866 A3 19990805
WO 1999-CA736 W 19990809
US 2001-849057 A1 20010504

OTHER SOURCE(S): MARPAT 132:180871
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Peptides I [B = H, (un)substituted aryl, aralkyl, heterocyclyl, or alkylheterocyclyl, acyl R4CO, carboxylate R4O2C, amide R4NR5CO, thioamide R4NR5C(S), or sulfonyl group R4SO2, where R4 = (un)substituted alkyl, cycloalkyl, cycloalkoxy, amino, aralkyl, or heterocyclyl, with proviso that R4 .noteq. cycloalkoxy for amides or thioamides; R5, Y = H, alkyl; R3 = (un)substituted alkyl, cycloalkyl, or alkylcycloalkyl; R2 = (un)substituted cycloalkyl-, aryl-, aralkyl-, or heterocyclylmethyl, -amino, -oxy, or -thio; R1 = H; alkyl, cycloalkyl, alkenyl, or alkynyl, all optionally substituted with halogen] or their racemates, diastereoisomers, and optical isomers were prepd. as hepatitis C virus (HCV) inhibitory tripeptides. Thus, compd. II was prepd. via peptide coupling reactions in soln. and showed IC50 < 0.5 .mu.M in the recombinant HCV NS3 protease/NS4A cofactor peptide radiometric assay.

IT 259214-89-6P 259214-91-0P 259214-92-1P
259214-93-2P 259214-94-3P 259214-97-6P
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 259217-00-0P 259217-01-1P 259217-02-2P
 259217-03-3P 259217-04-4P 259217-05-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of hepatitis C inhibitory tripeptides)

IT 259214-66-9P 259214-69-2P 259214-72-7P
 259214-82-9P 259214-83-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. of hepatitis C inhibitory tripeptides)

L16 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:126924 HCAPLUS

DOCUMENT NUMBER: 130:168665

TITLE: Preparation of hepatitis C inhibitory peptides

INVENTOR(S): Llinas-Brunet, Montse; Poupart, Marc-Andre; Rancourt, Jean; Simoneau, Bruno; Tsantrizos, Youla; Wernic, Dominik

PATENT ASSIGNEE(S): Boehringer Ingelheim (Canada) Ltd., Can.

SOURCE: PCT Int. Appl., 158 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|--|----------|-----------------|----------|
| WO 9907733 | A2 | 19990218 | WO 1998-CA765 | 19980810 |
| WO 9907733 | A3 | 19990520 | | |
| W: | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, | | | |

CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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|------------|----|----------|----------------|----------|
| AU 9887956 | A1 | 19990301 | AU 1998-87956 | 19980810 |
| AU 757783 | B2 | 20030306 | | |
| EP 1003775 | A2 | 20000531 | EP 1998-939450 | 19980810 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI

| | | | | |
|---------------|----|----------|----------------|----------|
| JP 2001512743 | T2 | 20010828 | JP 2000-506235 | 19980810 |
| NZ 503262 | A | 20021025 | NZ 1998-503262 | 19980810 |
| MX 200001498 | A | 20001110 | MX 2000-1498 | 20000211 |

PRIORITY APPLN. INFO.: US 1997-55186P P 19970811
WO 1998-CA765 W 19980810

OTHER SOURCE(S): MARPAT 130:168665

AB Peptides B[NHCHR6CO]a[NHCHR5CO]bQCHR4C(:Z)NHCHR3COWNHCR1R1'COA (when Q is CH2 and a and b are 0, B is an amide deriv. or when Q is NH or alkylimino and a and b are 0 or 1, B is an acyl deriv.; R6 = carboxyalkyl; R5 = alkyl or carboxyalkyl; R4 = alkyl, cycloalkyl, alkylcycloalkyl; Z = oxo or thioxo; R3 = alkyl, carboxyalkyl, cycloalkyl, alkylcycloalkyl; W is an amino acid residue such as proline; R1' = H and R1 = alkyl, mercapto- or haloalkyl or R1' and R1 together form a 3- to 6-membered ring; A is hydroxy or a pharmaceutically acceptable salt or ester) were prepd. as hepatitis C virus inhibitors. Thus, Ac-Asp-D-Glu-Chg-Val-X-Nva-OH [Chg = cyclohexylglycine, X = 4(R)-(2-naphthylmethoxy)proline, and Nva = norvaline residue], prepd. by step-wise couplings in soln., showed IC50 = 0.028 .mu.M in the NS3 protease/NS4A cofactor peptide radiometric assay.

IT 220425-88-7P 220425-89-8P 220425-94-5P
220426-02-8P 220426-07-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of hepatitis C inhibitory peptides)

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DICTIONARY FILE UPDATES: 24 FEB 2004 HIGHEST RN 654050-72-3

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| 3 | RN | 652160-88-8 | REGISTRY |
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| 104 | RN | 259221-43-7 | REGISTRY |
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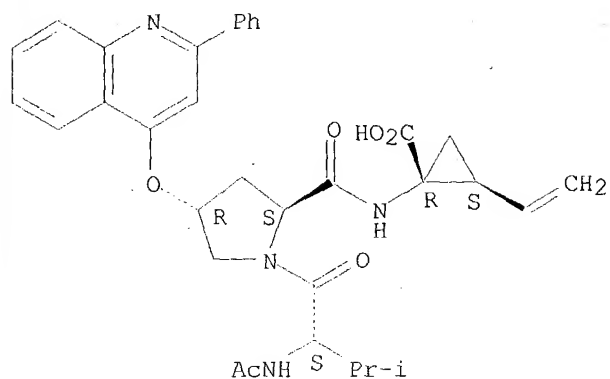
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341

L15 ANSWER 1 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN
RN 652160-91-3 REGISTRY
CN INDEX NAME NOT YET ASSIGNED

FS STEREOSEARCH
 MF C33 H36 N4 O6
 SR CA
 LC STN Files: CAPLUS

Absolute stereochemistry.

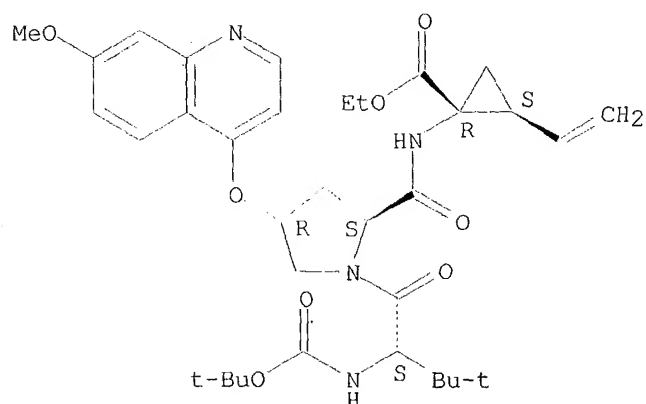


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L15 ANSWER 5 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 630424-40-7 REGISTRY
 CN Cyclopropanecarboxylic acid, N-[(1,1-dimethylethoxy)carbonyl]-3-methyl-L-valyl-(4R)-4-[(7-methoxy-4-quinolinyl)oxy]-L-prolyl-1-amino-2-ethenyl-, ethyl ester, (1R,2S)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C34 H46 N4 O8
 SR CA
 LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:16975

L15 ANSWER 12 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN

RN 607403-39-4 REGISTRY

CN Cyclopropanecarboxylic acid, N-[(1,1-dimethylethoxy)carbonyl]-3-methyl-L-valyl-(4R)-4-(4-quinolinyloxy)-L-prolyl-1-amino-2-ethenyl-, (1S,2R)- (9CI)
(CA INDEX NAME)

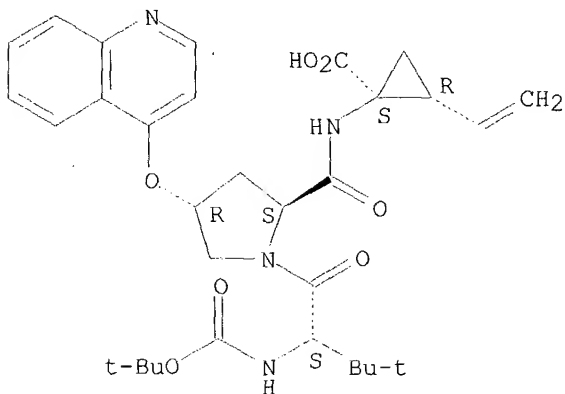
FS STEREOSEARCH

MF C31 H40 N4 O7

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:292471

L15 ANSWER 13 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN

RN 579472-70-1 REGISTRY

CN Cyclopropanecarboxylic acid, N-acetyl-L-.alpha.-aspartyl-D-.alpha.-glutamyl-(2S)-2-cyclohexylglycyl-3-methyl-L-valyl-(4R)-4-[(2-phenyl-4-quinolinyl)oxy]-L-prolyl-1-amino-2-ethenyl-, (1R,2S)- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

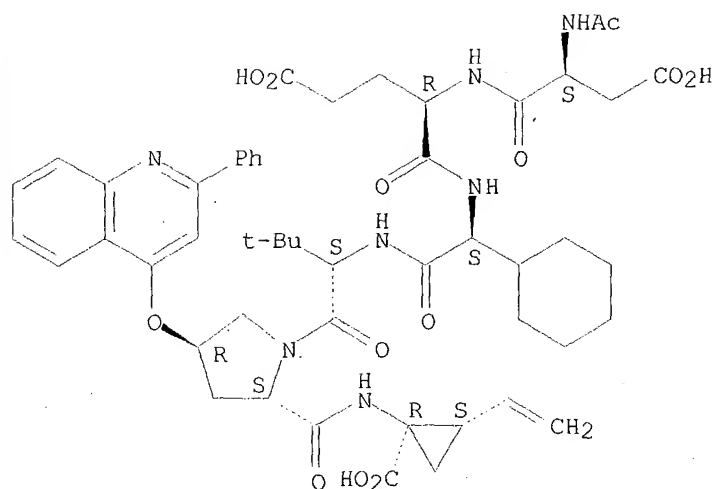
MF C51 H63 N7 O13

SR CA

LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



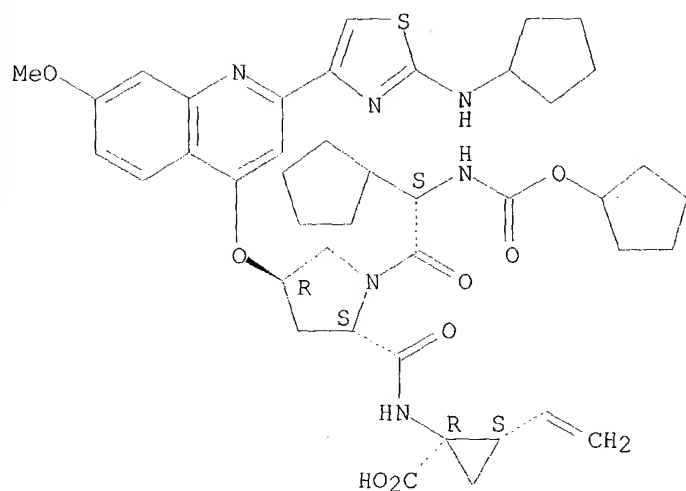
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:173244

L15 ANSWER 14 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN
RN 572925-06-5 REGISTRY
CN Cyclopropanecarboxylic acid, (2S)-2-cyclopentyl-N-
[(cyclopentyloxy)carbonyl]glycyl-(4R)-4-[[2-[2-(cyclopentylamino)-4-
thiazolyl]-7-methoxy-4-quinolinyl]oxy]-L-prolyl-1-amino-2-ethenyl-,
(1R,2S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C42 H52 N6 O8 S
CI COM
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:246223

REFERENCE 2: 139:164980

L15 ANSWER 21 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN

RN 572924-99-3 REGISTRY

CN Cyclopropanecarboxylic acid, N-[(cyclobutyloxy)carbonyl]-3-methyl-L-valyl-
(4R)-4-[[2-[2-(cyclopentylamino)-4-thiazolyl]-7-methoxy-4-quinolinyl]oxy]-
L-prolyl-1-amino-2-ethenyl-, (1R,2S)-, mono(trifluoroacetate) (9CI) (CA
INDEX NAME)

FS STEREOSEARCH

MF C40 H50 N6 O8 S . C2 H F3 O2

SR CA

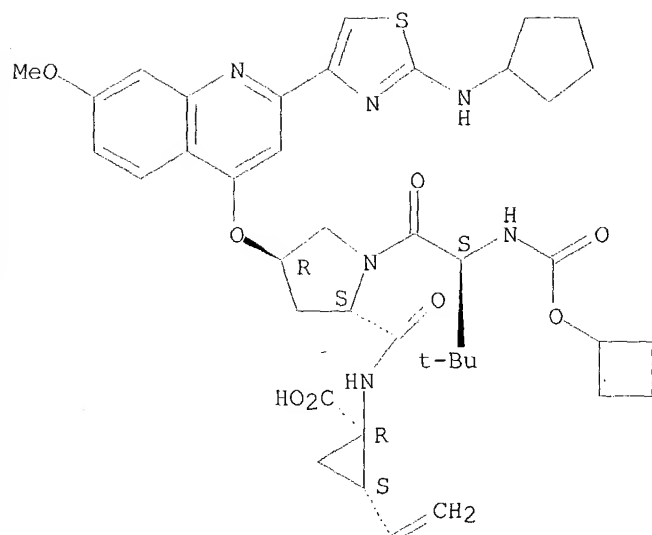
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

CM 1

CRN 572924-98-2

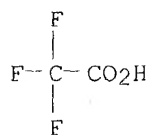
CMF C40 H50 N6 O8 S

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3.O2



2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:246223

REFERENCE 2: 139:164980

L15 ANSWER 51 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN

RN 572918-60-6 REGISTRY

CN Cyclopropanecarboxylic acid, 1-[[[(2S,4R)-1-[(2S)-2-[[[(1,1-dimethylethoxy)carbonyl]amino]-1-oxoheptyl]-4-[(7-methoxy-2-phenyl-4-quinolinyl)oxy]-2-pyrrolidinyl]carbonyl]amino]-2-ethenyl-, (1R)- (9CI)
(CA INDEX NAME)

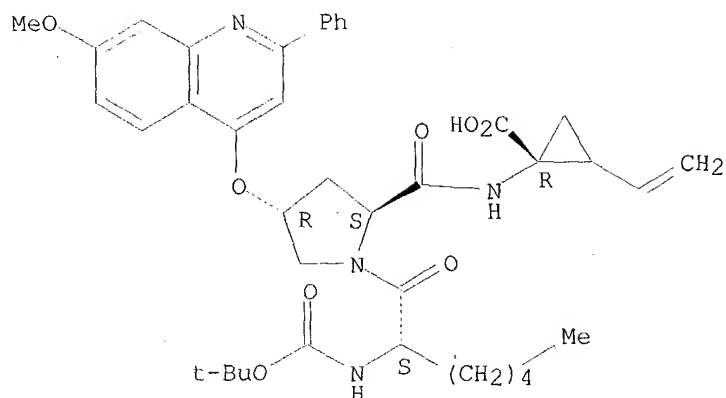
FS STEREOSEARCH

MF C39 H48 N4 O8

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:143358

L15 ANSWER 53 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN

RN 552335-61-2 REGISTRY

CN 2-Quinolinecarboxylic acid, 4-[[[(3R,5S)-1-[(2S)-2-[[[(1,1-dimethylethoxy)carbonyl]amino]-1-oxo-8-nonenyl]-5-[[[(1R,2S)-2-ethenyl-1-(ethoxycarbonyl)cyclopropyl]amino]carbonyl]-3-pyrrolidinyl]oxy]-7-methoxy-, methyl ester (9CI) (CA INDEX NAME)

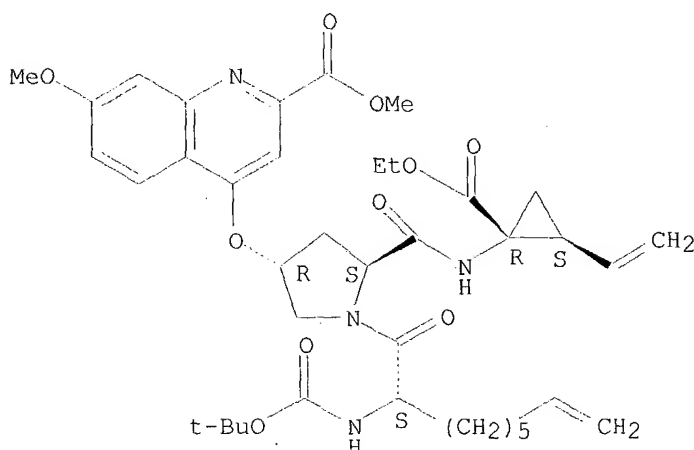
FS STEREOSEARCH

MF C39 H52 N4 O10

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

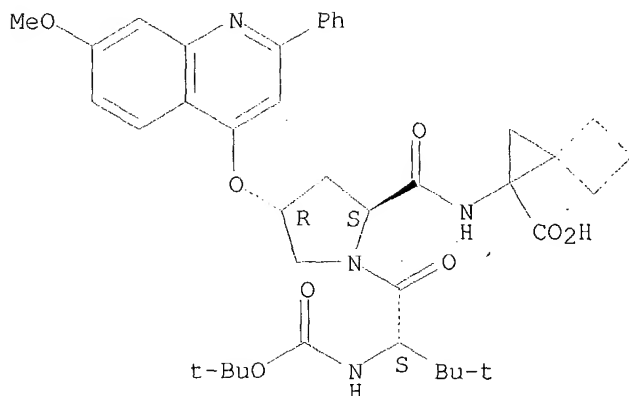
1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:69527

L15 ANSWER 60 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 445306-43-4 REGISTRY
 CN Spiro[2.3]hexane-1-carboxylic acid, N-[(1,1-dimethylethoxy)carbonyl]-3-methyl-L-valyl-(4R)-4-[(7-methoxy-2-phenyl-4-quinolinyl)oxy]-L-prolyl-1-amino- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C39 H48 N4 O8
 SR CA
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



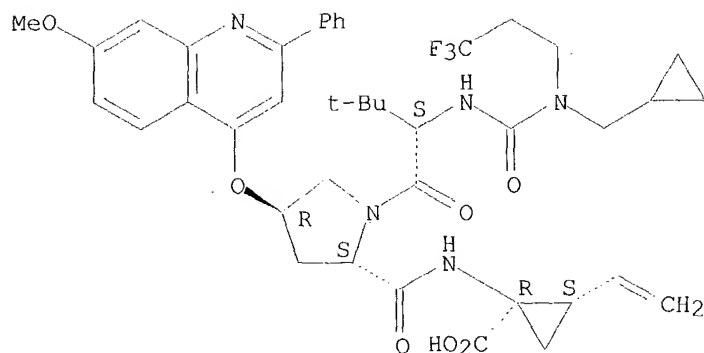
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:155180

L15 ANSWER 64 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 445305-99-7 REGISTRY
 CN Cyclopropanecarboxylic acid, N-[(cyclopropylmethyl)(3,3,3-trifluoropropyl)amino]carbonyl]-3-methyl-L-valyl-(4R)-4-[(7-methoxy-2-phenyl-4-quinolinyl)oxy]-L-prolyl-1-amino-2-ethenyl-, (1R,2S)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C41 H48 F3 N5 O7
 SR CA
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:155180

L15 ANSWER 72 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN

RN 357293-17-5 REGISTRY

CN Cyclopropanecarboxylic acid, (2S)-N-acetyl-2-cyclohexylglycyl-L-valyl-(4R)-4-[(6-methoxy-4-quinolinyl)oxy]-L-prolyl-1-amino- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

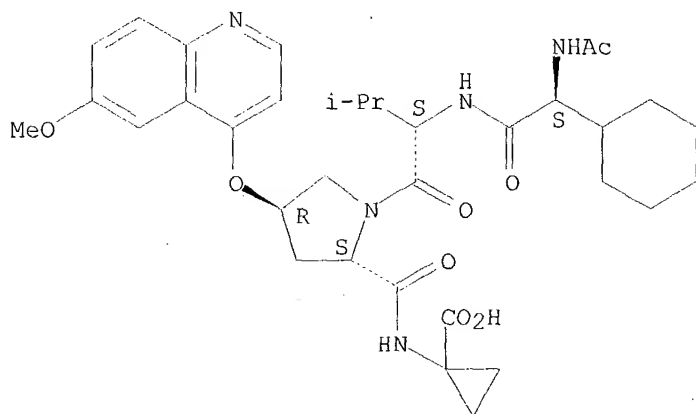
MF C34 H45 N5 O8

SR CA

LC STN Files: CA, CAPLUS, CASREACT

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

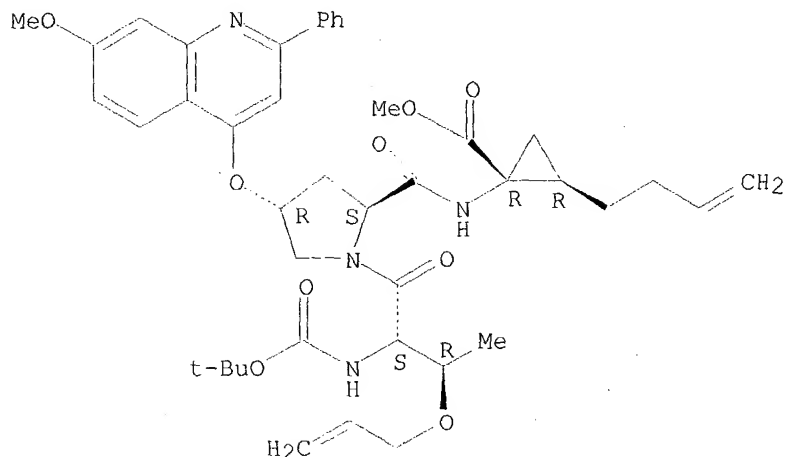
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 135:195782

L15 ANSWER 80 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN

RN 300831-65-6 REGISTRY
 CN Cyclopropanecarboxylic acid, N-[(1,1-dimethylethoxy)carbonyl]-O-2-propenyl-L-threonyl-(4R)-4-[(7-methoxy-2-phenyl-4-quinolinyl)oxy]-L-prolyl-1-amino-2-(3-butenyl)-, methyl ester, (1R,2R)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C42 H52 N4 O9
 SR CA
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139;197768

REFERENCE 2: 133;296659

L15 ANSWER 88 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN

RN 259221-63-1 REGISTRY

CN Cyclopropanecarboxylic acid, (2S)-2-cyclohexyl-N-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]glycyl-3-methyl-L-valyl-(4R)-4-[(7-methoxy-2-phenyl-4-quinolinyl)oxy]-L-prolyl-1-amino-2-ethenyl-, (1R,2S)- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

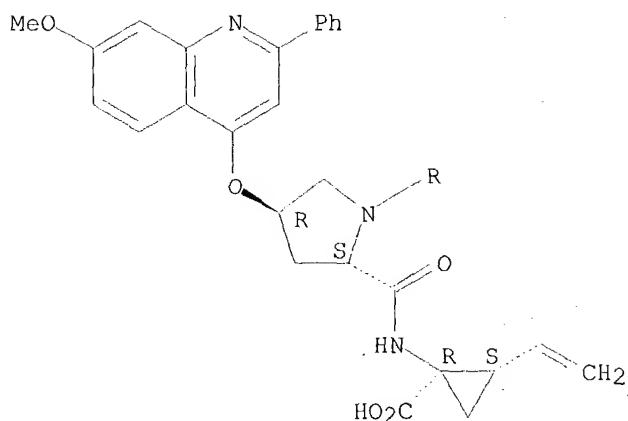
MF C53 H62 N6 O9 S

SR CA

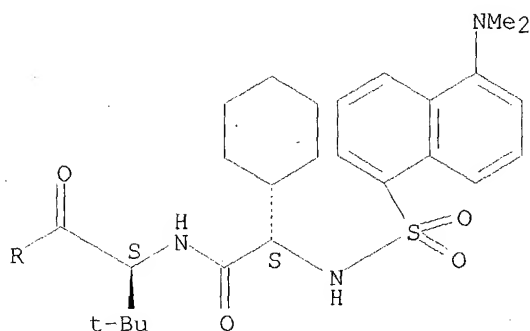
LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



PAGE 2-A



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

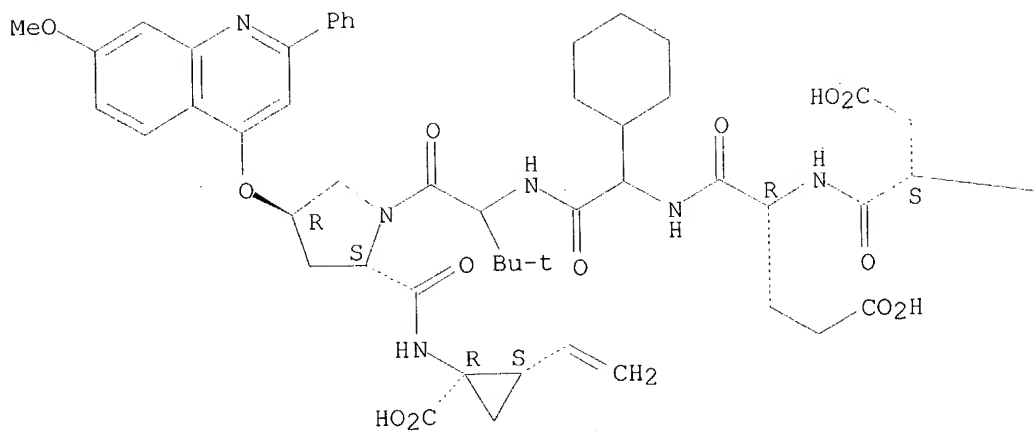
REFERENCE 1: 132:175808

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L15  ANSWER 100 OF 341  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   259221-51-7  REGISTRY
CN   Cyclopropanecarboxylic acid, N-[[5-(dimethylamino)-1-
      naphthalenyl]sulfonyl]-L-.alpha.-aspartyl-D-.alpha.-glutamyl-2-
      cyclohexylglycyl-3-methylvalyl-(4R)-4-[(7-methoxy-2-phenyl-4-
      quinolinyl)oxy]-L-prolyl-1-amino-2-ethenyl-, (1R,2S)- (9CI)  (CA INDEX
      NAME)
FS   PROTEIN SEQUENCE; STEREOSEARCH
MF   C62 H74 N8 O15 S
SR   CA
LC   STN Files:  CA, CAPLUS
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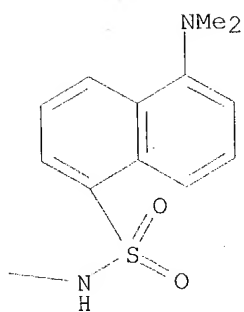
RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

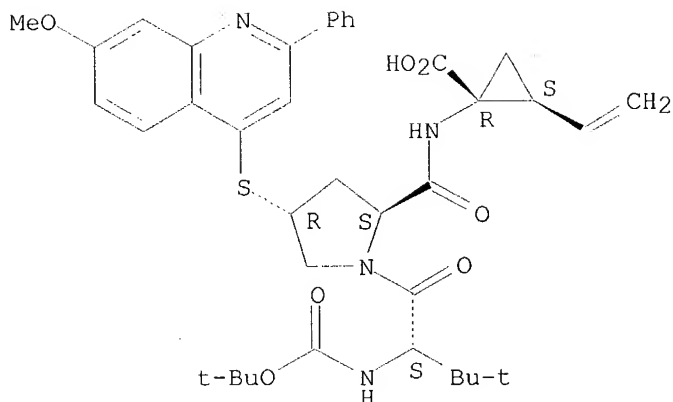


1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 132:175808

L15 ANSWER 134 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 259217-05-5 REGISTRY
 CN Cyclopropanecarboxylic acid, N-[(1,1-dimethylethoxy)carbonyl]-3-methyl-L-valyl-(4R)-4-[(7-methoxy-2-phenyl-4-quinolinyl)thio]-L-prolyl-1-amino-2-ethenyl-, (1R,2S)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C38 H46 N4 O7 S
 SR CA
 LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.



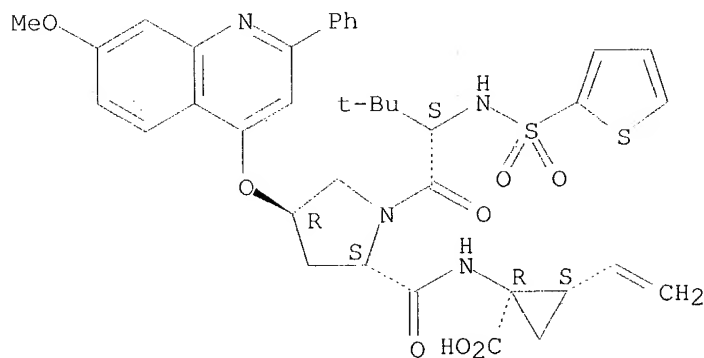
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 132:180871

L15 ANSWER 140 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN
RN 259216-99-4 REGISTRY
CN Cyclopropanecarboxylic acid, 3-methyl-N-(2-thienylsulfonyl)-L-valyl-(4R)-4-
[(7-methoxy-2-phenyl-4-quinolinyl)oxy]-L-prolyl-1-amino-2-ethenyl-,
(1R,2S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
ME C37 H40 N4 O8 S2
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

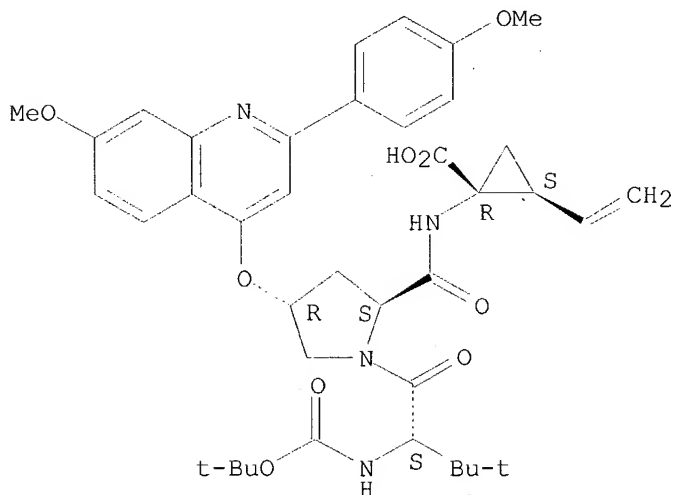
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 132:180871

L15 ANSWER 200 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN
RN 259216-39-2 REGISTRY

CN Cyclopropanecarboxylic acid, N-[(1,1-dimethylethoxy)carbonyl]-3-methyl-L-valyl-(4R)-4-[[7-methoxy-2-(4-methoxyphenyl)-4-quinolinyl]oxy]-L-prolyl-1-amino-2-ethenyl-, (1R,2S)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C39 H48 N4 O9
 SR CA
 LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.



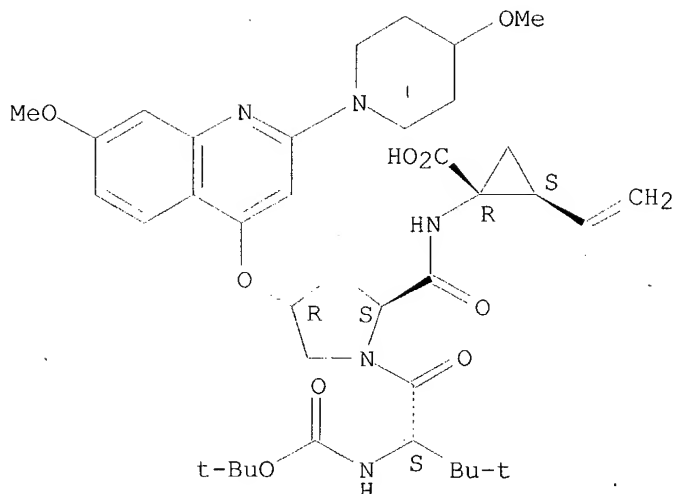
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 132:180871

L15 ANSWER 240 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 259215-99-1 REGISTRY
 CN Cyclopropanecarboxylic acid, N-[(1,1-dimethylethoxy)carbonyl]-3-methyl-L-valyl-(4R)-4-[[7-methoxy-2-(4-methoxy-1-piperidinyl)-4-quinolinyl]oxy]-L-prolyl-1-amino-2-ethenyl-, (1R,2S)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C38 H53 N5 O9
 SR CA
 LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 132:180871

L15 ANSWER 250 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN

RN 259215-89-9 REGISTRY

CN Cyclopropanecarboxylic acid, N-[(1,1-dimethylethoxy)carbonyl]-3-methyl-L-valyl-(4R)-4-[[7-methoxy-2-(2-methyl-4-thiazolyl)-4-quinolinyl]oxy]-L-prolyl-1-amino-2-ethenyl-, (1R,2S)- (9CI) (CA INDEX NAME)

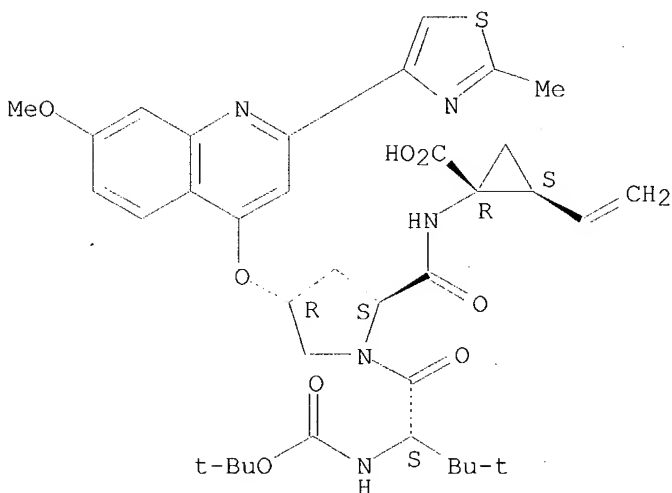
FS STEREOSEARCH

MF C36 H45 N5 O8 S

SR CA

LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.



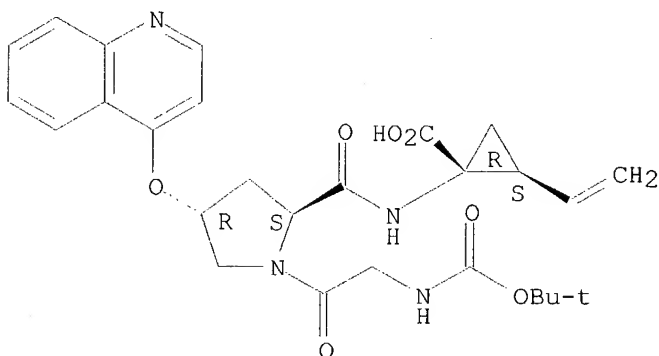
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 132:180871

L15 ANSWER 300 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN
RN 259215-39-9 REGISTRY
CN Cyclopropanecarboxylic acid, N-[(1,1-dimethylethoxy)carbonyl]glycyl-(4R)-4-(4-quinolinyloxy)-L-prolyl-1-amino-2-ethenyl-, (1R,2S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H32 N4 O7
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.



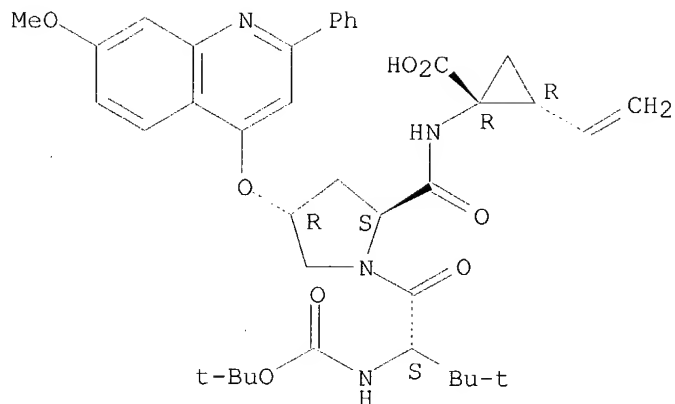
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 132:180871

L15 ANSWER 326 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN
RN 259214-97-6 REGISTRY
CN Cyclopropanecarboxylic acid, N-[(1,1-dimethylethoxy)carbonyl]-3-methyl-L-valyl-(4R)-4-[(7-methoxy-2-phenyl-4-quinolinyloxy)-L-prolyl-1-amino-2-ethenyl-, (1R,2R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H46 N4 O8
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

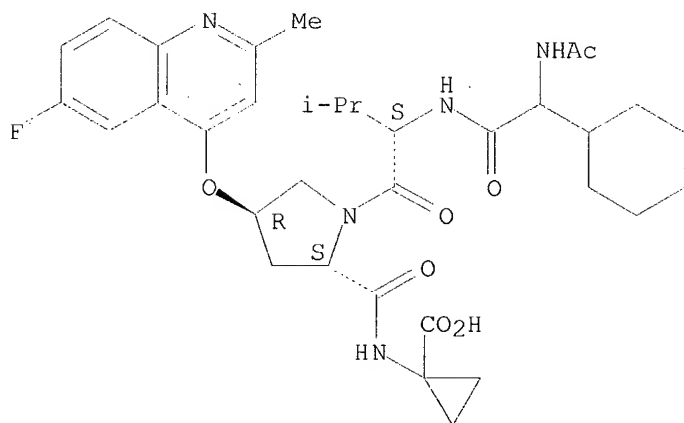
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 132:180871

L15 ANSWER 337 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN
RN 220426-07-3 REGISTRY
CN Cyclopropanecarboxylic acid, N-acetyl-2-cyclohexylglycyl-L-valyl-(4R)-4-
[(6-fluoro-2-methyl-4-quinolinyl)oxy]-L-prolyl-1-amino- (9CI) (CA INDEX
NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C34 H44 F N5 O7
SR CA
LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

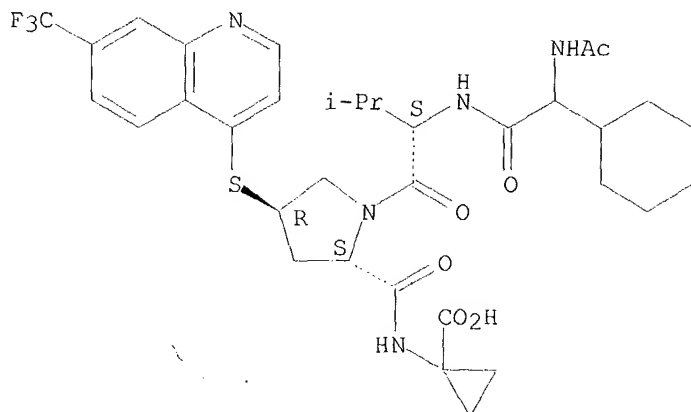
REFERENCE 1: 130:168665

L15 ANSWER 341 OF 341 REGISTRY COPYRIGHT 2004 ACS on STN

RN 220425-88-7 REGISTRY
 CN Cyclopropanecarboxylic acid, N-acetyl-2-cyclohexylglycyl-L-valyl-(4R)-4-
 [[7-(trifluoromethyl)-4-quinolinyl]thio]-L-prolyl-1-amino- (9CI) (CA -
 INDEX NAME)
 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C34 H42 F3 N5 O6 S
 SR CA
 LC STN Files: CA, CAPLUS

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:168665